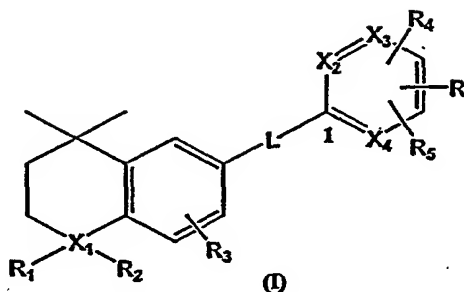


CLAIMS

- 5 1- A compound having a general formula (I) :



wherein:

10

R is $-\text{C}(\text{O})\text{NR}_7\text{R}_8$, $-(\text{CXY})_t\text{C}(\text{O})\text{NR}_7\text{R}_8$, $-\text{C}(\text{O})\text{C}(\text{O})\text{NHMe}$, $-(\text{C}=\text{C})\text{C}(\text{O})\text{NR}_8\text{R}_9$, $-\text{C}(\text{O})\text{CF}_3$, or another Zn-chelating-group, with the proviso that R is not an acidic group or an ester derivative, $-\text{COOR}_9$ or salt thereof, R_7 is a group of formula $-\text{OH}$, $-\text{OR}_9$, 2-aminophenyl and R_8 is selected from hydrogen, C_{1-6} alkyl; R_9 is
 15 independently selected from hydrogen or C_{1-6} alkyl ; t is 1, 2 or 3 (preferably 1), X and Y, which are identical or different, represent an hydrogen or halogen atom (preferably F),

X_1 represents a carbon, oxygen, nitrogen or sulphur atom,

20

R_1 and R_2 represent independently or form together:

- . a C_{1-6} alkyl group, in particular methyl or ethyl groups, when X_1 is an atom of carbon,
- . nothing, when X_1 is an atom of oxygen or an atom of sulphur,

- . one or two atoms of oxygen, when X_1 is an atom of sulphur (the case of a sulfoxide $-\text{SO}-$ or a sulphone $-\text{SO}_2-$), or
- . one atom of hydrogen, an alkyl, aryl or aralkyl group, when X_1 is an atom of nitrogen (the case of an amino $-\text{NH}$, -an N-alkyl, N-aryl or N-aralkyl group);

5

X_2 and X_3 , which are identical or different, represent CH, an atom of oxygen or an atom of nitrogen, or $X_2=X_3$ may be a single atom of sulphur, oxygen or nitrogen, or in the case where X_2 is an atom of oxygen and X_3 an atom of nitrogen, C_1 and X_4 represent a single one and same carbon atom, so that the

10 ring carrying X_2 and X_3 can be an isoxazole ring,

X_4 can be CH or a nitrogen atom,

R_4 and R_5 , which are identical or different, represent a hydrogen atom, a halogen atom, more particularly a fluorine atom, a C_{1-6} alkyl group, a group of formula -

15 OH, $-\text{NH}_2$, $-\text{NHR}_6$, $-\text{OR}_6$, $-\text{SR}_6$, $-(\text{CF}_2)_n\text{CF}_3$, where n is an integer from 0 to 10, and whenever possible their salts with physiologically tolerated acids;

R_6 represents a hydrogen atom, a C_{1-6} alkyl group, a fluoroalkyl group having

20 from 1 to 6 carbons atoms and from 3 to 7 fluorine atoms, an aryl group or an aralkyl group;

R_3 has the same definition as R_4 and R_5 ;

25 L is a linker and represents a bivalent radical either linear or cyclic, either saturated or unsaturated, more particularly L represents a bivalent radical derived from an alkane, alkene, alkyne or, aromatic or not, cyclic containing hydrocarbon group having from 1 to 12 carbon atoms, another bivalent radical of the following formula $-\text{O}-$, $-\text{CO}-$, $-\text{CO}-\text{NH}-$, $-\text{NH}-\text{CO}-$, $-\text{NH}-\text{CO}-\text{NH}-$, $-\text{CF}_2-\text{CO}-\text{NH}-$,

30 $-\text{C}(\text{XY})-\text{CO}-\text{NH}-\text{CH}_2-$, $-\text{NH}-\text{CO}-\text{CO}-\text{NH}-$, $-\text{NH}-\text{CO}-\text{CO}-\text{NH}-\text{CH}_2-$, $-\text{SO}_2\text{NH}-$, $-\text{NHSO}_2-$, $-\text{SO}_2\text{NCH}_3-$, $-\text{NCH}_3\text{SO}_2-$, $-\text{NR}_6-$, $-\text{C}(=\text{NOH})-$, or a mixture thereof; R_6 being as defined above, optionally the bivalent radical is substituted, in particular by at least one C_{1-6} alkyl group;

X and Y, which are identical or different, represent an hydrogen or halogen atom (preferably F),

5 its tautomers, optical and geometrical isomers, racemates, salts, hydrates and mixtures thereof.

2- A compound according to claim 1, wherein the groups identified in claim 1 are substituted with at least one substituent, which may be selected from the group consisting in : a hydrogen atom, a halogen atom (preferably F, Cl, or Br), a
10 hydroxyl group, a C₁₋₁₀alkyl group, an alkenyl group, an C₁₋₁₀alkanoyl group, a (C₁-C₁₀)alkoxy group, a (C₁-C₁₀)alkoxycarbonyl group, an aryl group, an aralkyl group, an arylcarbonyl group, a mono- or poly-cyclic hydrocarbon group, a -NHCO(C₁-C₆)alkyl group, -NO₂, -CN, a -Nrr' group or a trifluoro(C₁-C₆)alkyl group, r and r', which are identical or different, are as defined in claim 1.

15

3- A compound according to claim 1 or 2, wherein R is -C(O)NR₇R₈ or - (CXY)_tC(O)NR₇R₈, in particular wherein R₈ is an hydrogen atom and R₇ is an hydroxyl group or a 2-aminophenyl group, preferably with X and Y are both halogen atoms and t is 1.

20

4. A compound according to claim 3, wherein R is an hydroxamic acid group (- (C=O)-NH-OH), a 2,2-difluoro-N-hydroxyacetamido group (-CF₂-(C=O)-NH-OH), a N-(2-aminophenyl)acetamido group.

25

5- A compound according to claim 4, wherein R is an electrophilic ketone, in particular -(C=O)-CF₃ or α-ketoamides, for instance -(C=O)-(C=O)-NHMe.

6- A compound according to claim 4, wherein R is in para position or meta position of C1, R is preferably in para position of C1.

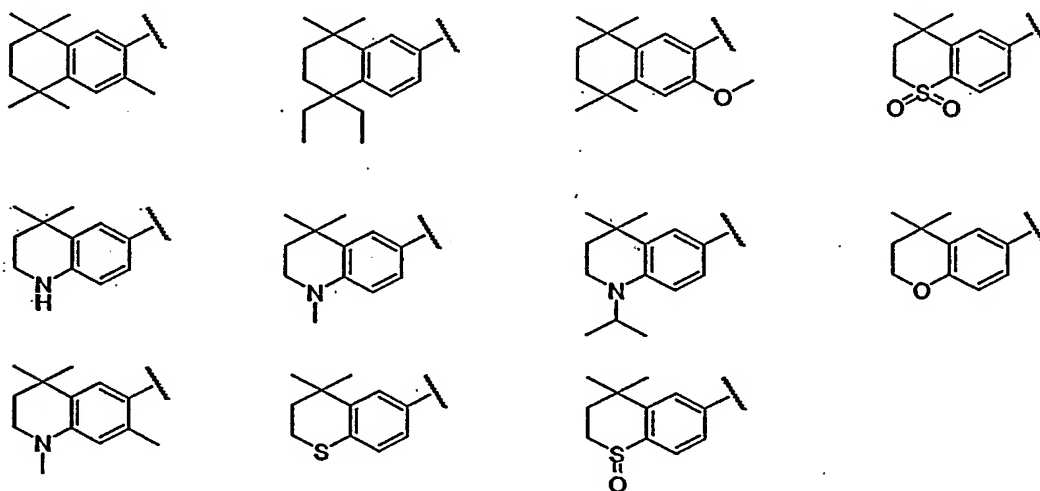
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7- A compound according to one of the preceding claims, wherein L represents -CO-NH-, -NH-CO-, -CH=CH- (cis or trans forms), -CF₂-CO-NH-, -CF₂-CO-NH-CH₂-, or -NH-CO-CO-NH-.

5 8- A compound according to any one of the preceding claims, wherein R₃ is an hydrogen atom, OR₆, in particular methoxy, or a C₁₋₆alkyl group, in particular methyl.

9- A compound according to any one of the preceding claims, wherein R₃ is on
10 position 2 of the substituted naphthalene derivative.

10- A compound according to any one of the preceding claims, wherein the ring carrying X₁ is selected from :



15

11- A compound according to one of the preceding claims, wherein the ring carrying X₂, X₃ and X₄ is selected from phenyl, pyridinyl, pyrimidinyl, isoxazolyl, thiophenyl, furanyl, pyrrolyl, pyrazolyl, imidazolyl, isothiazolyl, thiazolyl, thienyl, thienooxazolyl and triazinyl rings.
20

12- A compound according to one of the preceding claims, wherein the ring carrying X₂, X₃ and X₄ is phenyl, optionally substituted by a halogen atom, more particularly a fluorine atom, a C₁₋₆alkyl group, a group of formula -OH, or OR₆.

13- A compound, which is selected from the group consisting of :

N-(4-(Hydroxycarbamoyl)phenyl)-5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalene-2-carboxamide

5 *N*-(4-(2-Aminophenylcarbamoyl)phenyl)-5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalene-2-carboxamide

N-(1,2,3,4-Tetrahydro-1,1,4,4-tetramethylnaphthalen-6-yl)-*N*'-hydroxyterephthalamide

10 4-((*E*)-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-6-yl)vinyl)-*N*-hydroxybenzamide

4-((*Z*)-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-6-yl)vinyl)-*N*-hydroxybenzamide

4-(2,2-difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)acetamido)-*N*-hydroxybenzamide

15 3-(2,2-difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)acetamido)-*N*-hydroxybenzamide

4-((2,2-difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)acetamido)methyl)-*N*-hydroxybenzamide

20 *N*-(4-((hydroxycarbamoyl)difluoromethyl)phenyl)-5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalene-2-carboxamide

N-(4-Hydroxycarbamoyl-phenyl)-*N*'-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-naphthalen-2-yl)-oxalamide

N-(4-hydroxycarbamoyl-benzyl)-*N*'-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-naphthalen-2-yl)-oxalamide

14- A compound, which is selected from the group consisting of :

25 4-(2,2-Difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)acetamido)-*N*-hydroxybenzamide

N-(1,2,3,4-Tetrahydro-1,1,4,4-tetramethylnaphthalen-6-yl)-*N*'-hydroxyterephthalamide

30 4-((2,2-Difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)acetamido)methyl)-*N*-hydroxybenzamide

N-(4-(Hydroxycarbamoyl)phenyl)-5,6,7,8-tetrahydro-5,5,8,8-tetramethylnaphthalene-2-carboxamide

- 15- A compound according to any one of the preceding claims for use as a medicine.
- 5 16- A pharmaceutical composition comprising at least one compound according to any one of the preceding claims 1-14 and a pharmaceutically acceptable vehicle or support.
- 10 17- A composition according to the preceding claim, for the treatment of conditions mediated by HDAC, such as cancers, in particular promyelocytic leukaemia, other diseases associated with abnormal cell proliferation, such as psoriasis.
- 15 18- A composition according to the preceding claim 16, for the treatment of central and peripheral nervous system diseases and neurodegenerative diseases associated with an excitotoxicity, such as Huntington's disease, such as polyglutamine expansion diseases, Alzheimer disease, Parkinson disease, multiple sclerosis, neuronal ischemia and amyotrophic lateral sclerosis (ALS).
- 20 19- A composition according to the preceding claim 16, for the treatment of fibrosis, e.g. liver fibrosis and liver chirrrosis.
- 25 20- A composition according to claim 17, wherein the cancer is selected from promyelocytic leukaemia, prostate cancer, ovarian cancer, pancreas cancer, lung cancer, breast cancer, liver cancer, head and neck cancer, colon cancer, bladder cancer, non-Hodgkin 's lymphoma cancer and melanoma.
- 21- A composition according to claim 16, for reducing cancer cell proliferation.